CME Article

Updated Recommendations for Reducing Vertical Hiv Transmission

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Learning Objectives

i. To describe preconceptual counseling of women with hiv infection.
ii. To understand the role of short course antiretroviral therapy to reduce the risk of perinatal hiv transmission.
iii. To describe the role of hiv counseling and rapid or expedited hiv testing for women who present in labor with unknown hiv status.

Medical management of pregnant women with hiv infection and strategies to rduce the risk of its transmission to their infants are evolving areas of practice. In May 2001, the U. S. Public Health Service Perinatal Guidelines Working Group again updated the guidelines that were originally developed in 1998. This report summarizes the updated information that has been published since "Prevention of Perinatal Hiv Tranmission" appeared in the March 2001 issue of *New Jersey Medicine*.

Preconception Counseling

The revised guidelines contain a new section on preconception counseling of women with hiv infection. This section notes that many women with hiv infection do know their diagnosis at the time they become pregnant and are often already on antiretroviral therapy. The guidelines recommend that, where desired, a woman be offered an effective method of contraception until she reaches an optimal health status for pregnancy. Prior to pregnancy, she should be educated and counseled about the risks of perinatal transmission, strategies she can use to reduce those risks, and the potential effects of hiv and its treatment on her pregnancy. Initiation or modification of her antiretroviral therapy prior to conception can help her avoid agents with potential toxicity for the fetus (such as efaverenz or hydroxyurea) and choose agents effective in reducing transmission and achieving a stable, maximally suppressed maternal viral load. Preconception counseling also provides the opportunity to evaluate the woman's overall health, including her risk of opportunistic infections and any needed prophylaxis; to evaluate her nutritional status; to screen for maternal psychological or substance-abuse problems; and to perform the standard preconception evaluation that would be offered to any woman.

Antiretroviral Drugs

The guidelines also update recommendations for the use of antiretroviral (arv) drugs to reduce peri-

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Table1. Comparison of Intrapartum/Postpartum Regimens for HIV-Infected Women in Labor Who Have Had No Prior Antiretroviral Therapy

DRUG REGIMEN	SOURCE OF EVIDENCE	MATERNAL INTRAPARTUM	INFANT POSTPARTUM
NEVIRAPINE	Clinical trial, Africa; compared to oral ZDV given intrapatrtum and for one week to the infant	Single 200 mg oral dose at onset of labor	Single 2 mg/kg oral dose at age 48–72 hours*
ZDV/3tc	Clinical trial, Africa; compared to placebo	ZDV 600 mg orally at onset of labor, followed by 300 mg orally every three hours until delivery AND 3TC 150 mg orally at onset of labor, followed by 150 mg orally every 12 hours until delivery	ZDV 4 mg/kg orally every 12 hours AND 3TC 2 mg/kg orally every 12 hours for 7 days
ZDV	Epidemiologic data, U.S.; compared to no ZDV treatment	2 mg/kg intravenous bolus, followed by continuous infusion of 1 mg/kg/hr	2 mg/kg orally every 6 hours for 6 weeks
ZDV AND NEVIRAPINE	Theoretical	ZDV 2 mg/kg intravenous bolus, followed by continuous infusion of 1 mg/kg/hr until delivery AND Nevirapine single 200 mg oral dose at onset of labor	ZDV 2 mg/kg orally every 6 hours for 6 weeks AND Nevirapine single 2 mg/kg oral dose at age 48–72 hours

*If the mother received nevirapine less than 1 hour prior to delivery, the infant was given 2 mg/kg oral nevirapine as soon as possible after birth and again at 48–72 hours.

DRUG REGIMEN	DATA ON TRANSMISSION	ADVANTAGES	DISADVANTAGES
Nevirapine	Transmission at 6 weeks 12% with nevirapine compared to 21% with ZDV, a 47% (95% Cl, 20%–64%) reduction	Inexpensive; oral regimen; simple, easy to administer; can give directly observed treatment	Unknown efficacy if mother has nevirapine-resistant virus
ZDV/3tc	transmission at 6 weeks 10% with ZDV/ 3TC compared to 17% with placebo, a 38% reduction	Oral regimen; compliance easier than 6 weeks of ZDV alone as infant regimen is only 1 week	Potential toxicity of multiple drug exposure
ZDV	Transmission 10% with ZDV compared to 27% with no ZDV treatment, A 62% (95% CL, 19%–82%) reduction	Has been standard recommendation before clinical trial results	Requires intravenous administration and availability of ZDV intravenous formulation
ZDV AND Nevirapine	No data	Potential benefit if maternal virus is resistant to either nevirapine or ZDV; Synergistic inhibition of HIV replication with combination *in vitro*	Requires intravenous administration and availability of ZDV intravenous formulation; Compliance with 6-week infant ZDV regimen; Unknown efficacy and limited toxicity data

natal HIV transmission. For women who have not previously been treated with ARV, the guidelines recommend the three-part zidovudine (ZDV) regimen, beginning after the first trimester. Since a lower viral load seems to be associated with a reduced risk of perinatal HIV transmission, the combination of ZDV with additional ARV drugs is the recommended treatment for infected women with HIV RNA copy levels that are more than 1,000, regardless of clinical or immune status. A woman with HIV who is already receiving ARV and whose pregnancy is identified after the first trimester should continue treatment, and ZDV should be a component of the treatment regimen whenever possible. Zidovudine is recommended during the intrapartum and newborn periods regardless of the mother's earlier treatment. Recommendations for resistance testing for pregnant women with HIV infection are the same as for other patients-acute HIV infection and virologic failure or suboptimal viral suppression after ARV is initiated. Data from clinical trials has not shown that the addition of additional ARV drugs, such as nevirapine, at the time of delivery, for women with less than optimal viral suppression, provides additional protection against perinatal transmission.

The Centers for Disease Control and Prevention (CDC) recommends that any woman who presents in labor with the delivery team unaware of her HIV status should receive counseling and be offered HIV testing. (This offer of HIV testing is also required by New Jersey state regulations.) The use of a rapid or expedited HIV diagnostic test could provide results quickly enough to allow short-course antiretroviral therapy to reduce the risk of perinatal HIV transmission.

For the woman with HIV infection who presents in labor with no prior ARV therapy, the U.S. Public Health Service's Perinatal Guidelines Working Group continue to recommend one of four therapeutic regimens (see table 1). Infants who are born to mothers who have not taken ARV drugs during pregnancy or intrapartum should receive ZDV for six weeks, and therapy should be initiated, whenever possible, within 6 to 12 hours of birth. A comparison of the options for short-course therapy is shown in table 1. Diagnostic testing of these infants should be initiated as soon as possible.

Prenatal Care

It is not unusual for an HIV-infected pregnant woman to present in labor with the delivery team unaware of her HIV status and with no prior ARV therapy. In New Jersey, preliminary data suggests that the majority of children (7 out of 8, 88%) who became infected with HIV through perinatal transmission in 1999 and 2000 were born to women who presented in labor with the delivery team unaware of their HIV status. A major contributing factor to this absence of information is the lack of or inadequacy of prenatal care. Approximately 25% of HIV-infected pregnant women in New Jersey do not receive prenatal care.

The New Jersey Department of Health and Senior Services (NJDHSS) is addressing these missed opportunities for prevention by collaborating with two ad hoc advisory committees. The committees developed a standard of care incorporating the recommendations of the CDC and U.S. Public Health Service's Perinatal Guidelines Working Group. The NJDHSS standard of care has been disseminated and is available on the NJDHSS's website. The standard of care can be used by all hospitals providing obstetrical care. The recommendation is to provide HIV counseling and offer rapid or expedited testing for women who present in labor with unknown HIV serostatus. Those who test positive would then be offered short course therapy to reduce the risk of vertical HIV transmission. The goal of this statewide approach is to collaborate with physicians, nurses, hospitals, and other stakeholders for maximal reduction of vertical HIV transmission in New Jersey.

The U.S. Public Health Service's Perinatal Guidelines Working Group meets regularly to update these guidelines. The updated guidelines can be read at the HIV–AIDS Treatment Information Service web site (www.hivatis.org). The site offers the opportunity to join a listserv that will automati-

cally alert its members when any of the guidelines (perinatal, pediatric, or adult) are updated. *NJM*

References

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2. S. Paul et al. "Prevention of Perinatal HIV Transmission," *New Jersey Medicine* 98, no. 3 (March 2001): 23–31.

3. New Jersey Administrative Code 8:61–3.1.

4. Centers for Disease Control and Prevention. "Revised Public Health Service Recommendations for Human Immunodeficiency Virus Screening of Pregnant Women," draft dated October 20, 2000.

5. Centers for Disease Control and Prevention. "Success in Implementing Public Health Service Guidelines to Reduce Perinatal Transmission of HIV—Louisiana, Michigan, New Jersey, and South Carolina, 1993, 1995, and 1996," *MMWR* 47 (1998): 688–691.

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"Updated Recommendations for Reducing Vertical HIV Transmission"

1. Counseling to reduce the risk of vertical HIV transmission should begin at which of the following times for women with HIV infection?
   A. Preconceptual
   B. First trimester
   C. Second trimester
   D. Third trimester
   E. Postpartum

2. Ideally, antiretroviral therapy to reduce the risk of vertical HIV transmission should start at which of the following gestational ages?
   A. First trimester
   B. Second trimester
   C. Third trimester
   D. Labor/delivery

3. Which of the following is recommended for women who present in labor with unknown HIV status?
   A. HIV counseling
   B. HIV rapid or expedited testing
   C. Short course therapy if HIV test is positive
   D. All of the above

4. Which of the following regimens is recommended for HIV-infected women in labor who have had no prior antiretroviral therapy?
   A. Nevirapine 200mg po at onset of labor + single 2mg/kg oral dose at age 48–72 hours for the infant
   B. ZDV 600 po at onset of labor followed by 300 mg po q 3 hours until delivery + ZDV 4mg/kg orally q 12 hours x 7 days for the infant
   C. ZDV 2mg/kg IV bolus followed by continuous infusion 1mg/kg/hr until delivery + 2mg/kg orally every 6 hours x 6 weeks for the infant.
   D. All of the above

5. Which of the following antiretroviral agents is recommended as part of the regiment to reduce the risk of vertical HIV transmission, whenever possible?
   A. Efavirenz
   B. Lamivudine
   C. Nevirapine
   D. Zidovudine

Answer Sheet

"Updated Recommendations for Reducing Vertical Hiv Transmission"

Darken the correct answers

1. [A] [B] [C] [D] [E] 2. [A] [B] [C] [D] 3. [A] [B] [C] [D]
4. [A] [B] [C] [D] 5. [A] [B] [C] [D]

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